

Preliminary Amendment

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Applicant: Salman Baig et al.

Serial No.: 10/018,936

Confirmation No.: 8674

Filed: October 19, 2001

For: *CYSTEINE PROTEASE AND INHIBITORS FOR PREVENTION AND TREATMENT OF NEUROCYSTICERCOSIS*

$\beta 2$

Hundreds of publications have now reported the efficacy of DNA vaccines in small and large animal models of infectious diseases, cancer and autoimmune diseases (J. Donnelly et al., Annu. Rev. Immunol. 15:617 (1997)). Vaccine dosages for humans can be readily extended from the murine models by one skilled in the art of genetic immunization, and a substantial literature on genetic immunization of humans is now available to the skilled practitioner. For example, Wang et al. (Science 282:476-480 (1998)) vaccinated humans with plasmid DNA encoding a malaria protein, and the same group has developed a plan for manufacturing and testing the efficacy of a multigene *Plasmodium falciparum* liver-stage DNA vaccine in humans (Hoffman et al., Immunol. Cell Biol. 75:376 (1997)). In general, the polynucleotide vaccine of the invention is administered in dosages that contain the smallest amount of polynucleotide necessary for effective immunization. It is typically administered to human subjects in dosages containing about 20 μ g to about 2500 μ g plasmid DNA; in some instances 500 μ g or more of plasmid DNA may be indicated. Typically the vaccine is administered in two or more injections at time intervals, for example at four week intervals.

Please replace the paragraph beginning at page 31, line 22, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

$\beta 3$

In the end, *Taenia* cysts may have become sensitized to a balance where a certain level of IgG in the host serum was actually beneficial metabolically, but too much could be destructive, immunologically. Perhaps there is a baseline physiological IgG level which is beneficial (IgG uptake in *T. crassiceps* cysts is shown to be saturable at physiological serum levels (Siebert et al., Exp. Parasitol. 48:164-174 (1979))). Thus, *Taenia* cysts may have a need for a certain level of

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IgGs for immune exploitation, but are harmed by concentration beyond this.

Perhaps, this is why the cysteine protease, which is highly antigenic (Example III), is not located on the cyst wall surface, but is rather *within* the cyst wall.

Consequently, the cysts may have evolved molecular mechanisms to control this balance. For example, a secretory *Taenia* glycoprotein (Villa et al., Parisotol. 112:561-570 (1996)) appears to modulate the shift from a host T helper 1 (Th1) cellular mediated immune response to a humoral T helper 2 response (Th2), favoring increased antibody production which may be used by the parasites for nutrition (this shift may also aid the parasites in avoiding a destructive Th1 cellular response, for which they have no defenses). Alternatively, diminished secretion of these molecules may slow down the shift from Th1 to Th2 allowing the parasites another means to control their immunological environment (and thus, physiological IgG levels).

B3
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